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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,439	04/17/2001	Therese de Bizemont	017753-154	5851
21839	7590	04/07/2004	EXAMINER	
BURNS DOANE SWECKER & MATHIS L L P POST OFFICE BOX 1404 ALEXANDRIA, VA 22313-1404				SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
	1635

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/836,439	Applicant(s) DE BIZEMONT ET AL.
	Examiner Richard Schnizer, Ph. D	Art Unit 1635

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) The period for reply expires 3 months from the mailing date of the final rejection.
 b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
 ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. The proposed amendment(s) will not be entered because:
 - (a) they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) they raise the issue of new matter (see Note below);
 - (c) they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. Newly proposed or amended claim(s) ____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 1,17,18,21,30 and 39.

Claim(s) withdrawn from consideration: 13-16,19,22-29 and 31-38.

8. The drawing correction filed on ____ is a) approved or b) disapproved by the Examiner.

9. Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.

10. Other: _____.

Continuation of 3. Applicant's reply has overcome the following rejection(s): claims 1, 17, 18, 21, 30, 39 for indefiniteness, claim 1 for lack of adequate written description.

Continuation of 5. does NOT place the application in condition for allowance because: The specification fails to enable the claims as amended. Applicant addresses the rejection at pages 23-24 of the response, noting that the claims as amended are limited to certain target genes. Applicant relies upon Andrieu et al (unpublished), Behar-Cohen (2004), and Davies et al (2003) for evidence of enablement. The Andrieu reference purportedly presents evidence of gene conversion and expression of a corrected protein *in vivo* in mouse retina. However, this reference, in which the inventors are coauthors, does not appear to be published, and has not been presented in the form of a signed declaration under 37 CFR 1.132. As such it is only hearsay, and is not persuasive as evidence. The Behar-Cohen abstract reports a chimeroplasty-mediated gene conversion of a mutation in phosphodiesterase subunit B in a mouse retina *in vivo*. The information disclosure statement filed by Applicant on 3/18/04 lists the Behar-Cohen abstract but does not indicate a publication date. The abstract itself bears a handwritten citation that reads "ISOPT, Monte Carlo, Monaco, 3/11-3/14, 2004", in apparent reference to a meeting presentation. The Office executed a search for this document but did not locate it in the available electronic databases. In view of this fact, and the fact that Applicant's information disclosure statement fails to indicate that the reference was published, it is considered to be unpublished, and similar to the Andrieu references, is considered to be hearsay. In any event, the abstract fails to provide relevant evidence of enablement in view of the skepticism in the art at the time of the invention. The only evidence of gene conversion presented in the abstract is expression of "b phospho-diesterase" by immunohistochemistry. However, the abstract fails to disclose whether or not the antibodies used could discriminate between mutant and wild type forms of the protein, and so provides no convincing evidence of enablement. The Davies (2003) document examines delivery of DNA/RNA hybrids across the sclera by electric fields. However, as discussed in the rejection, although chimeroplasty has been highly unpredictable in terms of reproducibility, the prior art does not identify poor oligonucleotide delivery as an explanation for this problem. Furthermore, it is not clear that iontophoresis results in better delivery of chimeroplasts than do cationic lipid transfection, electroporation, or microinjection. It follows that one of skill in the art would not reasonably expect to improve the predictability of chimeroplasty through the use of iontophoresis as a delivery technique. In view of the highly unpredictable state of the art of chimeroplasty, as established in the rejection, and the failure of the specification to teach those of skill in the art how to overcome this unpredictability, the rejection is maintained.



DAVE T. NGUYEN
PRIMARY EXAMINER